Preventing Diabetes in American Indian Communities

Diabetes incidence can be reduced by lifestyle interventions aimed at weight loss, diet change, and increased physical activity, according to several randomized clinical trials (RCTs) (1–5). Similarly, diabetes incidence rates were reduced in RCTs of metformin, acarbose, troglitazone, rosiglitazone, and pioglitazone (1,4,6–9). These RCTs enrolled nondiabetic adults who were at high risk of developing type 2 diabetes by virtue of having one of more of these characteristics: overweight or obesity, elevated fasting glucose, and impaired glucose tolerance in an oral glucose tolerance test. These lifestyle or drug interventions reduced diabetes incidence rates substantially, with risk reductions ranging from about 25–75%. Diabetes incidence was reduced by 58% during the 2.8-year initial phase of the largest such lifestyle intervention trial, the U.S. Diabetes Prevention Program (DPP) (1). This occurred among all the major race/ethnic groups in the DPP, including American Indians.

Because of this dramatic result and the disproportionate burden of type 2 diabetes among American Indians, the U.S. Congress appropriated funds to implement lifestyle interventions patterned on the DPP starting in 2006 in 36 American Indian or Alaska Native communities. The resulting Special Diabetes Program for Indians Diabetes Prevention (SDPI-DP) demonstration project is described in this issue (10). The SDPI-DP was designed to deliver prevention services to a population in need, rather than as another RCT, because RCTs had already shown the efficacy of lifestyle intervention to prevent or delay diabetes in high risk persons. Furthermore, the segments of the U.S. population most affected by type 2 diabetes, especially American Indians who have contributed so much to diabetes research (11), deserve to benefit from the results of diabetes research.

It is difficult to quantify the benefits of the SDPI-DP and similar programs that are not RCTs and therefore have no built-in evaluation mechanism. Evaluation, therefore, must rely on historical controls or comparisons with similar programs. Unlike most other implementation programs, the SDPI-DP evaluated diabetes incidence as well as weight change. As in the RCTs, diabetes incidence was ascertained by periodic glucose tolerance testing of all participants who remained under follow-up. Comparable historical data from the same communities are not available.

The authors compared their diabetes incidence rate (4 per 100 person-years) with the placebo group rate of 11 per 100 person-years and the lifestyle group rate of 4.8 per 100 person-years in the DPP. This comparison is difficult because eligibility criteria for the SDPI-DP were much broader than for the DPP, and thus the SDPI-DP participants were probably at much lower risk of diabetes. For example, DPP eligibility required elevations of both fasting and postload plasma glucose, whereas SDPI-DP required only one value to be elevated, which conveys a much lower risk of diabetes (5,12). Mean baseline 2-h glucose was 164 mg/dL (9.1 mmol/L) in the DPP (1) and 159 mg/dL (8.8 mmol/L) in the Finnish Diabetes Prevention Study (3), but only 123 mg/dL (6.8 mmol/L) in SDPI-DP—substantially below the lower limit defining impaired glucose tolerance (7.8 mmol/L). Furthermore, it is not known what other metabolic or behavioral characteristics differed between SDPI-DP participants and those enrolled in RCTs. The most important difference may have been the high drop-out rate in the SDPI-DP (only 33% completed the 3-year assessment). By comparison, 92% of DPP participants completed a study visit within 5 months of the end of the 2.8-year follow-up (1). Weight loss in behavioral treatment programs is positively correlated with attendance at treatment sessions (13,14), suggesting that those losing less weight are less likely to complete follow-up. Similarly, participants who develop clinically diagnosed diabetes may lose interest in a prevention program and not follow-up for glucose testing in the program (i.e., data are probably not missing at random). Therefore, estimated diabetes incidence might have been much higher in the SDPI-DP if it had been possible to assess diabetes incidence in all enrolled subjects (15).

Community implementation is very different from testing an intervention in an RCT, where participants are often highly motivated and resources are sufficient to provide interventions and retain participants. It is, therefore, informative to compare the SDPI-DP with other implementation programs evaluated using largely non-RCT methods. One recent systematic review summarized the 12-month weight loss effectiveness of 28 previously published implementation programs (16). Like the SDPI-DP, these prior efforts were designed to implement key elements of the DPP, which included targeting high-risk adults; goal setting and self-monitoring of dietary change, physical activity, and modest weight loss; and providing supportive accountability (typically via a lifestyle coach) to avoid pitfalls and solve problems leading to weight regain (17). However, the 28 previously published implementation programs differed greatly in participant selection, numbers of intervention sessions offered, inclusion of a control group, and how missing data were analyzed. Compared with SDPI-DP, participants in these programs were typically older (mean age 55.1 vs. 46.6 years in SDPI-DP) and more likely non-Hispanic white (70.9%). Similar to SDPI-DP, prior studies enrolled obese participants (mean BMI 34.0 kg/m^2 vs. 35.8 kg/m^2 in SDPI-DP) and women (69.9% vs. 74.5% in SDPI-DP). Across all these programs, mean weight change after 12 months among about 77% of total participants with follow-up data were −3.99% (95% CI −5.16 to −2.83). For comparison, we calculated weight change at 1 year and 3 years among the 1,503 (59% of those enrolled) and 834 (33%) SDPI-DP participants who completed 1 and 3 years of follow-up, respectively, from baseline data in Supplementary Table 1 and follow-up data in Table 2 of the article by Jiang et al. (10). The 1-year weight change (pounds) was (212.0 − 215.5)/215.5 = −1.6%. The 3-year change was (215.1 − 212.6)/212.6 = +1.2%. Weight change of this magnitude had no apparent effect on the diabetes incidence rate in the lifestyle intervention participants in the DPP

Table 1—*Characteristics of RCTs and implementation programs*

	RCT	Implementation program
Main purpose	Evaluate efficacy of intervention(s)	Provide service or evaluate effectiveness in practice settings
Current knowledge about the interventions	Effects not known	Presumed safe and effective, at least in some settings
Number of intervention arms	At least two	Usually one
Treatment assignment randomized	Yes (by individual or cluster)	Not typically*
Basis for evaluation	Internal: direct comparisons among randomized treatment arms	Variable and often difficult; comparison groups are usually external and inherently different in some respects
Internal validity	Strong	Variable; preplanned quasi-experimental designs preferable to post hoc analysis
External validity (generalizability)	Questionable; often low or difficult to determine	Often higher

*There are exceptions, such as cluster randomized pragmatic effectiveness trials or stepped-wedge designs in which implementation is performed immediately for randomized groups (e.g., clinics, cities) but delayed for others to enable a natural usual care control group.

(18). Weight loss and retention may have been better had SDPI-DP provided more intervention beyond the first 16 lifestyle lessons. Many studies have shown that short-term lifestyle interventions are insufficient for assuring weight maintenance (19). Indeed, long-range support was central to the original DPP intervention (17).

Key differences between RCTs and implementation programs such as the SDPI-DP are summarized in Table 1. These two activities have different primary purposes (evaluating interventions vs. providing service). Because RCTs include at least two interventions (one of which may be placebo or standard care) that are assigned randomly, they are optimal for evaluating interventions of unknown effect. By contrast, implementation programs provide service using interventions with (presumed) known benefits. RCTs provide internal validity, but the ability to generalize their findings is often unknown. Implementation programs may shed light on the effectiveness of interventions in practice, although their evaluation can be difficult, as illustrated by SDPI-DP.

In conclusion, through the SDPI-DP, the Indian Health Service has continued its admirable tradition of translating medical research findings into practice in challenging settings—often in isolated, rural, and economically deprived areas. The Indian Health Service has greatly improved the quality of service for treating diabetes and its complications since 1998 through the Special Diabetes Program for Indians (20,21). This high level of service is being extended to diabetes prevention, although important challenges remain. The SDPI-DP's strongest contribution is in showing that components of the DPP core curriculum can be adapted for delivery to a large and diverse American Indian population. Although the lack of a comparison group and high loss to follow-up temper conclusions about its long-range effectiveness, these findings should fuel further exploration of how such programs might be improved or integrated with other preventive efforts to reach more individuals and engage them over longer periods of time to prevent type 2 diabetes and its complications.

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DOI: 10.2337/dc12-2635

Acknowledgments—W.C.K. is supported by the Intramural Research Program of the National Institute of Diabetes and Digestive and Kidney Diseases. R.T.A. receives funding for diabetes prevention research from the National Institute of Diabetes and Digestive and Kidney Diseases (R18DK079855) and Centers for Disease Control and Prevention (U58DP002718), and he is supported by the Clinical and Translational Sciences Award Program under UL1TR000150.

No potential conflicts of interest relevant to this article were reported.

References

1. Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403
2. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 1997;20:537–544
3. Tuomilehto J, Lindström J, Eriksson JG, et al.; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343–1350
4. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V; Indian Diabetes Prevention Programme (IDPP). The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia 2006;49:289–297
5. Saito T, Watanabe M, Nishida J, et al.; Zensharen Study for Prevention of Lifestyle Diseases Group. Lifestyle modification and prevention of type 2 diabetes in overweight Japanese with impaired fasting glucose levels: a randomized controlled trial. Arch Intern Med 2011;171:1352–1360
6. Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M; STOP-NIDDM Trial Research Group. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet 2002;359:2072–2077
7. Knowler WC, Hamman RF, Edelstein SL, et al.; Diabetes Prevention Program Research Group. Prevention of type 2 diabetes with troglitazone in the Diabetes Prevention Program. Diabetes 2005;54:1150–1156

8. Gerstein HC, Yusuf S, Bosch J, et al.; DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet 2006;368:1096–1105
9. DeFronzo RA, Tripathy D, Schwenke DC, et al.; ACT NOW Study. Pioglitazone for diabetes prevention in impaired glucose tolerance. N Engl J Med 2011;364:1104–1115
10. Jiang L, Manson SM, Beals J, et al. Translating the Diabetes Prevention Program into American Indian and Alaska Native communities: results from the Special Diabetes Program for Indians Diabetes Prevention demonstration project. Diabetes Care 2013;36:2027–2034
11. Knowler WC, Pettitt DJ, Saad MF, Bennett PH. Diabetes mellitus in the Pima Indians: incidence, risk factors and pathogenesis. Diabetes Metab Rev 1990;6:1–27
12. Edelstein SL, Knowler WC, Bain RP, et al. Predictors of progression from impaired glucose tolerance to NIDDM: an analysis of six prospective studies. Diabetes 1997;46:701–710
13. Wadden TA, Foster GD, Letizia KA, Stunkard AJ. A multicenter evaluation of a proprietary weight reduction program for the treatment of marked obesity. Arch Intern Med 1992;152:961–966
14. Venditti EM, Bray GA, Carrion-Petersen ML, et al.; Diabetes Prevention Program Research Group. First versus repeat treatment with a lifestyle intervention program: attendance and weight loss outcomes. Int J Obes (Lond) 2008;32:1537–1544
15. Ware JH. Interpreting incomplete data in studies of diet and weight loss. N Engl J Med 2003;348:2136–2137
16. Ali MK, Echouffo-Tcheugui J, Williamson DF. How effective were lifestyle interventions in real-world settings that were modeled on the Diabetes Prevention Program? Health Aff (Millwood) 2012;31:67–75
17. Diabetes Prevention Program (DPP) Research Group. The Diabetes Prevention Program (DPP): description of lifestyle intervention. Diabetes Care 2002;25:2165–2171
18. Hamman RF, Wing RR, Edelstein SL, et al., for the Diabetes Prevention Program Research Group. Effect of weight loss with lifestyle intervention on risk of diabetes. Diabetes Care 2006;29:2102–2107
19. Jeffery RW, Drewnowski A, Epstein LH, et al. Long-term maintenance of weight loss: current status. Health Psychol 2000;19(Suppl.):5–16
20. Burrows NR, Narva AS, Geiss LS, Engelgau MM, Acton KJ. End-stage renal disease due to diabetes among southwestern American Indians, 1990-2001. Diabetes Care 2005;28:1041–1044
21. Wilson C, Gilliland S, Cullen T, et al. Diabetes outcomes in the Indian health system during the era of the Special Diabetes Program for Indians and the Government Performance and Results Act. Am J Public Health 2005;95:1518–1522